REMARKS/ARGUMENTS

Claims 23, 25-28, 30 and 32-37 are active. Claims 1-22, 24, 29 and 31 have been cancelled. Page 13 of the specification has been amended to refer to version 20 of AL162497 (SEQ ID NO: 18) which the specification discloses as having a length of 143,409 bp. Claim 23 has been revised to convert a wherein clause into conventional step language using the gerund "assessing". Claims 33 and 35 have been further limited to avoid an objection based on the last part of page 55 of the specification which describes assessing risk before drug administration. Claim 36 has been revised to indicate that the method of assessing the risk of vesnarinone-induced granulocytopenia using the probe- or primer-based method of claim 23 may form a part of a larger method of assessing risk of granulocytopenia. Conventional methods for assessing risk of granulocytopenia which may be performed in conjunction with that of claim 23 include those described in the section bridging pages 2-3 of the specification. Other minor edits have been made to some claims to improve clarity. No new matter has been introduced.

The Applicants thank Examiner Strzelecka for reviewing the chart appended to the attached Declaration under 37 C.F.R. §1.132 with TQAS Witz and for indicating that it adequately depicts the locations of the polymorphisms described in the claim by reference to the specification as originally filed. Redundant description of the locations of the polymorphisms by reference to both AL162497 (SEQ ID NO: 18) and by the identification of primer sequences useful for amplifying SNPs was reviewed. It was indicated that in view of such description it would not be necessary to rely on Accession number XM_007095 for descriptive support of the claims. The Applicants were requested to revise the specification to add the sequence identifier "SEQ ID NO: 18" (which now appears on page 13).

Restriction/Election

The Applicants previously elected with traverse **Group I**, claims 1-8, 14, 15 and 19-22, directed to a method for assessing risk of drug-induced granulocytopenia, and the **species genetic polymorphism (e) (A29793G)**. The requirement has been made FINAL. The Applicants understand that additional species will be rejoined and examined upon an indication of allowability for a generic claim reading on the elected species. The Applicants respectfully request that the claims of the nonelected group(s) which depend from or otherwise include all the limitations of an allowed elected claim, be rejoined upon an indication of allowability for the elected claim, see MPEP 821.04.

Incorporation by Reference

The reference to AL162497 and XM_007095 was objected to as being an improper incorporation by reference under 37 C.F.R. §1.57(b), (c) or (d). The Applicants believe that this issue is now moot in view of the provisional acceptance of the chart shown in the attached Declaration, in view of the redundant ways to identify the locations of the polymorphisms described in the claims, and in view of the revision of page 13 of the specification to describe SEQ ID NO: 18.

Rejections—35 U.S.C. §112, first paragraph (OA, pages 3 and 5)

Claims 23, 25-27 and 29-31 were rejected under 35 U.S.C. 112, first paragraph, as lacking adequate written description on the ground that the specification as filed did not describe where the polymorphisms of the IRS2 gene are located. The issue is whether the original disclosure discloses the claimed invention as it pertains to the locations of particular polymorphisms correlated with vesnarinone-induced granulocytopenia. As discussed above,

the positions of the polymorphisms of the invention are described by reference to AL162497 (version 20) which corresponds to SEQ ID NO: 18.

AL162497 (version 20) is a long polynucleotide sequence of which a portion (base pairs 93,673-126,402) encodes the IRS-2 gene (specification, top of page 14). However, this sequence is an antisense sequence and thus depicts the antisense nucleotides corresponding to the coding sequence for IRS-2 protein. For example, the start codon in the antisense sequence of SEQ ID NO: 18 appears as ("cat") at base pair 126,402. The sense version of this codon would be "atg". Similarly, what is down-stream in the antisense sequence of AL162497 (SEQ ID NO: 18) is upstream in the coding sequence shown by SEQ ID NO: 19.

The polymorphisms described in the claims appear as follows in SEQ ID NO: 18:

(a) an oligonucleotide having a sequence including a genetic polymorphism that is C to A conversion at position 130,474 of SEQ ID NO: 18. Page 14, lines 19-20 disclose the polymorphism C-4587A: a C → A conversion. This is depicted in antisense sequence AL162497 as a G → T conversion at the relative position 4,587 up-stream (bp 130,474) from the antisense start codon at 126,402.

(b) an oligonucleotide having a sequence including a genetic polymorphism that is an AT deletion at positions 128,398-128,399 of SEQ ID NO: 18. Page 14, lines 19-20 disclose the polymorphism AT-2510del: an AT deletion. This is depicted in antisense sequence AL162497 as a TA deletion at the relative position 2,510 up-stream (bp 128,398-128,399) from the antisense start codon at 126,402.

(c) an oligonucleotide having a sequence including a gene polymorphism that is A to C conversion at position 127,051 of SEQ ID NO: 18; Page 14, lines 19-20 disclose the polymorphism A-1164C: an A → C conversion. This is depicted in antisense sequence AL162497 as a T → G conversion at the relative position 1,164 up-stream (bp 127,051) from the antisense start codon at 126,402.

(d) an oligonucleotide having a sequence including a gene polymorphism that is A to G conversion at position of 110,018 of SEQ ID NO: 18; Page 14, lines 19-20 disclose the polymorphism A15780G an A → G conversion. This is depicted in antisense sequence AL162497 as a T → C conversion at the relative position 15,870 down-stream (bp 110,018) from the antisense start codon at 126,402.

(e) an oligonucleotide having a sequence including a gene polymorphism that is A to G conversion at position 96,095 of SEQ ID NO: 18. Page 14, lines 19-20 disclose the polymorphism A29793G: an A → G conversion. This is depicted in antisense sequence AL162497 (SEQ ID NO: 18) as a T → C conversion at the relative position 29,793 down-stream (96,095 bp) from the antisense start codon at 126,402.

(f) an oligonucleotide having a sequence including a genetic polymorphism that is C deletion between positions 94,356-94,357 of SEQ ID NO: 18. Page 14, lines 19-20 disclose the polymorphism C31532del. This is depicted in antisense sequence AL162497 (SEQ ID NO: 18) as a G deletion at the relative position 31,532 down-stream (between bp's 94,356-94,357) from the antisense start codon at 126,402.

These polymorphisms are specifically and unambiguously identified by their relative positions with respect to the IRS-2 gene's start codon, see page 14 of the specification. This start codon itself is definitively identified as shown by attachments B at bp 516 which corresponds to the "a" in the start codon "atg". Attachment D also depicts the location of the start codon of this gene in its antisense form.

Thus, as of the filing date of this invention, one of skill in the art would have been able to clearly identify this start codon from publicly available information, including GenBank Accession No. AL162497 and GenBank Accession No. XM_007095. If the Examiner disagrees, the Applicants respectfully request that she explain why the locations of the polymorphisms of the invention could not have been unambiguously identified based on

accession number AL162497 (version 20) when read in light of the specification and other publicly available information as of the filing date. In view of the above explanations and the revision of the specification to identify GenBank Accession No. AL162497 (version 20) the Applicants respectfully submit that these rejections cannot be sustained.

Objection

Claim 33 and 35 were objected to as to form. This issue is now moot.

Objection

Claim 33, 35 and 36 were objected to under 37 C.F.R. §1.75(c). This issue is now moot.

Rejection--Obviousness-type Double Patenting

Claims 33, 35 and 36 were objected to as being substantial duplicates of claims 32, 34 and 32, respectively. This issue is moot in view of the amendments above which further limit these claims.

Rejection—35 U.S.C. §112, first paragraph

Claims 23, 25-28, 30 and 32-37 were rejected under 35 U.S.C. 112, first paragraph, as lacking adequate written description. This rejection may be withdrawn for the same reasons given above in view of the comparison chart provided in the attached Declaration.

Rejection—35 U.S.C. §112, first paragraph

Claims 23, 25-28, 30 and 32-37 were rejected under 35 U.S.C. 112, first paragraph, as lacking adequate written description. This rejection may be withdrawn for the same reasons given above in view of the comparison chart provided in the attached Declaration.

Conclusion

In view of the amendments and remarks above, the Applicants respectfully submit that this application is now in condition for allowance. An early notice to that effect is earnestly solicited.

Respectfully submitted,

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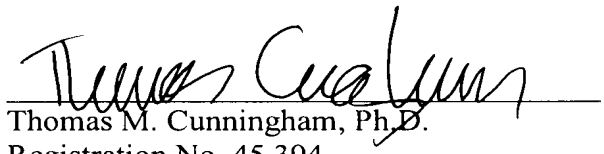

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